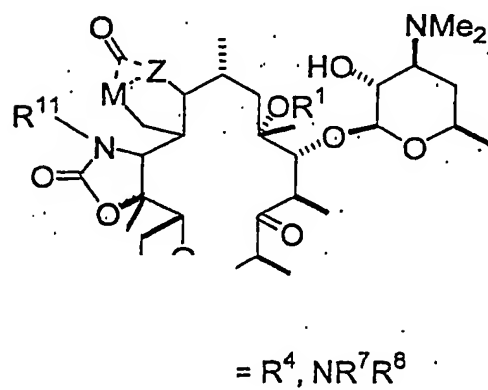
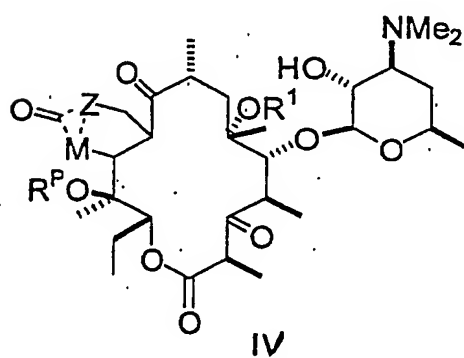
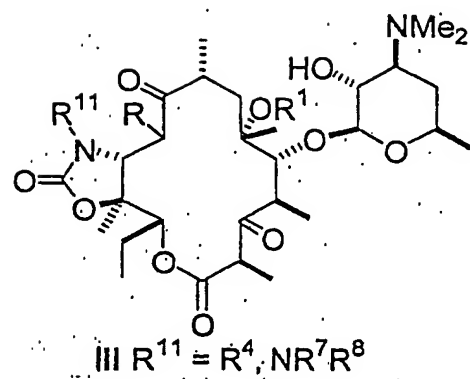
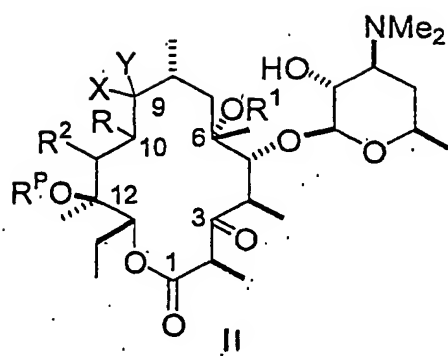


Claims:

1. 10-Substituted-10-desmethyl macrolides.
- 5 2. Macrolides as claimed in claim 1 wherein the 10-substituent is carbon-attached to the 10-carbon of the macrolide macrocyclic ring.
- 10 3. Macrolides as claimed in either of claims 1 and 2 wherein the 10-substituent is selected from methylene, substituted methyl, CHO and COOH and esters, amides and salts thereof.
- 15 4. Macrolides as claimed in claim 3 wherein the 10-substituent comprises an aryl group.
- 20 5. Macrolides as claimed in claim 1 substituted in the 2-position by methyl and hydrogen or fluorine; in the 3-position by oxo or optionally substituted hydroxy; in the 4-position by methyl; in the 5-position by an oxygen-attached desosamine; in the 6-position by methyl and an optionally substituted hydroxyl; in the 8-position by methyl and hydrogen or fluorine; in the 9-position by oxo; in the 10-position by methylene, CHO, substituted methyl, or carboxy or substituted carboxy; in the 11- and 12-positions by a group forming a fused ring at the 11, 12 and optionally 10-positions; at the 12-position additionally by a methyl group; and at the 13-position by an ethyl group.
- 25 6. Macrolides as claimed in claim 1 of formula II, III, IV or V
- 30



(1) methyl substituted with one or more substituents selected from the group consisting of

(i) CN,

(ii)

5 F,

(iii) CO_2R^3 wherein R^3 is selected from hydrogen, C_1 - C_3 -alkyl or aryl substituted C_1 - C_3 -alkyl, or heteroaryl substituted C_1 - C_3 -alkyl,

(iv)

10 OR^4 wherein R^4 is selected from hydrogen, C_1 - C_4 -alkyl or aryl substituted C_1 - C_4 -alkyl, or heteroaryl substituted C_1 - C_4 -alkyl, heterocycloalkyl and optionally substituted cycloalkyl, C_1 - C_3 -alkoxy- C_1 - C_3 -alkoxy, C_1 - C_4 -alkenyl or aryl substituted C_1 - C_4 -alkenyl, or heteroaryl substituted C_1 - C_4 -alkenyl, heterocycloalkyl and optionally substituted cycloalkyl, aryl or optionally substituted aryl, heteroaryl or optionally substituted heteroaryl,

15 (v) $\text{S(O)}_n\text{R}^3$ wherein $n = 0, 1$ or 2 and R^3 is as previously defined

20 (vi)

$\text{NR}^4\text{C(O)R}^3$ wherein R^3 and R^4 are as previously defined

(vii) $\text{NR}^4\text{C(O)NR}^5\text{R}^6$ wherein R^4 is defined as defined previously, and R^5 and R^6 are independently selected from

25 hydrogen, C_1 - C_3 -alkyl, C_1 - C_3 alkyl substituted with aryl, substituted aryl, heteroaryl, substituted heteroaryl

(viii) NR^7R^8 wherein R^7 and R^8 are independently selected from the group consisting of

(a) hydrogen

30 (b) C_1 - C_{12} -alkyl, and optionally substituted C_1 - C_{12} -alkyl

(c) C_2 - C_{12} -alkenyl, and optionally substituted C_2 - C_{12} -alkenyl

(d) C_2 - C_{12} -alkynyl, and optionally substituted C_2 - C_{12} -alkynyl

35 (e) aryl, and optionally substituted aryl

- (f) heteroaryl, and optionally substituted heteroaryl
(g) heterocycloalkyl, and optionally substituted heterocycloalkyl
(h) C₁-C₁₂ alkyl substituted with aryl, and optionally substituted with substituted aryl
(i) C₁-C₁₂ alkyl substituted with heteroaryl, and optionally substituted with substituted heteroaryl
(j) C₁-C₁₂ alkyl substituted with heterocycloalkyl, and with optionally substituted heterocycloalkyl, and
(k) R⁷ and R⁸ taken together with the atom to which they are attached from a 3-10- membered heterocycloalkyl ring which may contain one or more additional heteroatoms and may be substituted with one or more substituents independently selected from the group consisting of
(aa) halogen, hydroxy, C₁-C₃-alkoxy, alkoxy-C₁-C₃-alkoxy, oxo, C₁-C₃-alkyl, aryl and optionally substituted aryl, heteroaryl and optional substituted heteroaryl
(bb) CO₂R³ wherein R³ is as previously defined, and
(cc) C(O)NR⁵R⁶ wherein R⁵ and R⁶ are as previously defined,
(ix) aryl, and optionally substituted aryl, and
(x) heteroaryl, and optionally substituted heteroaryl,
(2) C₂-C₁₀-alkyl,
(3) C₂-C₁₀-alkyl substituted with one or more substituents selected from the group consisting of
(i) halogen,
(ii) OR⁴ wherein R⁴ is as defined previously
(iii) -CHO,
(iv) oxo,

- (v) NR^7R^8 wherein R^7 and R^8 are defined as previously
- (vi) $=\text{N}-\text{O}-\text{R}^4$ is wherein R^3 is as previously defined
- (vii) $-\text{CN}$
- 5 (viii) $-\text{S}(\text{O})_n\text{R}^3$ wherein $n = 0, 1$ or 2 and R^3 is as previously defined
- (ix) aryl, and optionally substituted aryl
- (x) heteroaryl, and optionally substituted heteroaryl
- 10 (xi) C_3-C_8 -cycloalkyl, and optionally substituted C_3-C_8 -cycloalkyl
- (xii) heterocycloalkyl, and optionally substituted heterocycloalkyl
- 15 (xiii) $\text{NR}^4\text{C}(\text{O})\text{R}^3$ where R^3 and R^4 are as previously defined
- (xiv) $\text{NR}^4\text{C}(\text{O})\text{NR}^5\text{R}^6$ wherein R^4 , R^5 and R^6 are as previously defined
- (xv) $=\text{N}-\text{NR}^7\text{R}^8$ wherein R^7 and R^8 are as previously defined
- 20 (xvi) $=\text{N}-\text{R}^4$ wherein R^4 is as previously defined
- (xvii) $=\text{N}-\text{NR}^4\text{C}(\text{O})\text{R}^3$ wherein R^3 and R^4 are as previously defined, and
- (xviii) $=\text{N}-\text{NR}^4\text{C}(\text{O})\text{NR}^5\text{R}^6$ wherein R^4 , R^5 and R^6 are as
- 25 previously defined,
- (4) C_2-C_{10} -alkenyl,
- (5) C_2-C_{10} -alkenyl substituted with one or more substituents selected from the group consisting of
- (i) halogen,
- 30 (ii) OR^4 wherein R^4 is as previously defined
- (iii) $\text{O}-\text{S}(\text{O})_n\text{R}^3$ where n and R^3 are as previously defined
- (iv) $-\text{CHO}$,
- (v) oxo,
- 35 (vi) $-\text{CO}_2\text{R}^3$ where R^3 is as previously defined
- (vii) $-\text{C}(\text{O})-\text{R}^4$ where R^4 is as previously defined

- (viii) -CN
(ix) aryl, and optionally substituted aryl
(x) heteroaryl, and optionally substituted heteroaryl
5 (xi) C₃-C₇-cycloalkyl
(xii) C₁-C₁₂-alkyl substituted with heteroaryl
(xiii) NR⁷R⁸ wherein R⁷ and R⁸ are as previously defined
(xiv) NR⁴C(O)R³ where R³ and R⁴ are as previously defined
(xv) NR⁴C(O)NR⁵R⁶ where R⁴, R⁵ and R⁶ are as previously
10 defined

(xvi) =N-O-R⁴ where R⁴ is as previously defined
(xvii) =N-NR⁷R⁸ wherein R⁷ and R⁸ are as previously defined
(xviii) =N-NR⁴ wherein R⁴ is as previously defined
15 (xix) =N-NR⁴C(O)R³ wherein R³ and R⁴ are as previously
defined, and
(xx) =N-NR⁴C(O)NR⁵R⁶ wherein R⁴, R⁵ and R⁶ are as previously
defined,

20 (6) C₂-C₁₀-alkynyl
(7) C₂-C₁₀-alkynyl substituted with one or more
substituents selected from the group consisting of
(i) trialkylsilyl
(ii)
25 halogen,
(iii) -CN
(iv)
OR⁴ where R⁴ is defined as previously
(v) -CHO,
30 (vi)
oxo,
(vii) -CO₂R³ where R³ is as previously defined
(viii) -C(O)NR⁵R⁶ wherein R⁵ and R⁶ are as previously
defined
35 (ix) NR⁷R⁸ wherein R⁷ and R⁸ are as previously defined
(x) O-S(O)_nR³ where n and R³ are as previously defined

- (xi) C₃-C₇-cycloalkyl
(xii) C₁-C₁₂-alkyl substituted with heteroaryl
(xiii) aryl, and optionally substituted aryl
(xiv) heteroaryl, and optionally substituted heteroaryl
5 (xv) NR⁴C(O)R³ where R³ and R⁴ are as previously defined
(xvi) NR⁴C(O)NR⁵R⁶ where R⁴, R⁵ and R⁶ are as previously defined
- (xvii) =N-O-R⁴ where R⁴ is as previously defined
10 (xviii) =N-NR⁷R⁸ wherein R⁷ and R⁸ are as previously defined
(xix) =N-NR⁴C(O)R³ wherein R³ and R⁴ are as previously defined, and
(xx) =N-NR⁴C(O)NR⁵R⁶ wherein R⁴, R⁵ and R⁶ are as previously defined,
15 defined,
- (8) cyclic substituents
(i) aryl, and optionally substituted aryl
(ii) heteroaryl, and optionally substituted heteroaryl
20 (iii) heterocycloalkyl, and optionally substituted heterocycloalkyl, and
(iv) C₃-C₇-cycloalkyl, and optionally substituted C₃-C₇-cycloalkyl, and
(9) C₁ substituents with the exception of 10-methyl
25 derivatives which are part of the above definitions under (1)
(i) -CHO
(ii) -CN
30 (iii) CO₂R³ wherein R³ is as previously defined
(iv) C(O)NR⁵R⁶ wherein R⁵ and R⁶ are as previously defined
(v) C(S)NR⁵R⁶ wherein R⁵ and R⁶ are as previously defined
(vi)
35 C(NR⁴)NR⁵R⁶ wherein R⁴, R⁵ and R⁶ are as previously defined

(vii) $\text{CH}=\text{N}-\text{O}-\text{R}^4$ wherein R^4 is as previously defined
(viii) $\text{CH}=\text{N}-\text{R}^4$ is wherein R^4 is as previously defined
(ix) $\text{CH}=\text{N}-\text{NR}^7\text{R}^8$ wherein R^7 and R^8 are as previously defined

5 (x)

$\text{CH}=\text{N}-\text{NR}^4\text{C}(\text{O})\text{R}^3$ wherein R^3 and R^4 are as previously defined, and

(xi) $\text{CH}=\text{N}-\text{NR}^4\text{C}(\text{O})\text{NR}^5\text{R}^6$ wherein R^4 , R^5 and R^6 are as previously defined;

10 R^1 is selected from the group consisting of

(1) H

(2) methyl

(3) methyl substituted with one or more substituents selected from the group consisting of

15 (i) F

(ii)

-CN

(iii) $-\text{CO}_2\text{R}^{11}$ where R^{11} is C_1 - C_3 -alkyl or aryl substituted C_1 - C_3 -alkyl, or heteroalkyl substituted C_1 - C_3 -alkyl

20 (iv) $-\text{C}(\text{O})\text{NR}^5\text{R}^6$ wherein R^5 and R^6 are defined as previously

(v) aryl, and optionally substituted aryl, and

(vi) heteroaryl, and optionally substituted heteroaryl

(4) C_2 - C_{10} -alkyl

25 (5) substituted C_2 - C_{10} -alkyl with one or more substituents selected from the group consisting of

(i) halogen,

(ii)

OR^4 where R^4 is defined as previously

30 (iii) C_1 - C_3 -alkoxy- C_1 - C_3 -alkoxy

(iv) $-\text{CHO}$

(v) oxo

(vi) NR^7R^8 wherein R^7 and R^8 are as previously defined

(vii) $=\text{N}-\text{O}-\text{R}^4$ where R^4 is as previously defined

35 (viii) $-\text{CN}$

(ix) $-\text{S}(\text{O})_n\text{R}^3$ where $n = 0, 1, \text{ or } 2$ and R^3 is as

previously defined

(x)aryl, and optionally substituted aryl

(xi) heteroaryl, and optionally substituted heteroaryl

5 (xii) C₃-C₈-cycloalkyl, and optionally substituted C₃-C₈-
cycloalkyl

(xiii) C₁-C₁₂-alkyl substituted with heteroaryl, and
optionally substituted heteroaryl

(xiv) heterocycloalkyl

(xv) NHC(O)R³ where R³ is as previously defined

10 (xvi) NHC(O)NR⁵R⁶ where R⁵ and R⁶ are as previously
defined

(xvii)=N-NR⁷R⁸ wherein R⁷ and R⁸ are as previously defined

(xviii) =N-R⁴ wherein R⁴ as previously defined, and

15 (xix)=N-NHC(O)R³ wherein R³ is as previously defined,

(4) C₁-C₁₀-alkenyl substituted with one or more
substituents selected from the group consisting of

(i) halogen,

(ii)

20 OR⁴ where R⁴ is as previously defined

(iii)-CHO

(iv)

oxo

(v) -S(O)_nR³ where n and R³ are as previously defined

25 (vi) -CN

(vii) -CO₂R³ where R³ is as previously defined

(viii)NR⁷R⁸ wherein R⁷ and R⁸ are as previously defined

(ix) =N-O-R⁴ where R⁴ is as previously defined

(x) -C(O)-R⁴ where R⁴ is as previously defined

30 (xi)

-C(O)NR⁵R⁶ wherein R⁵ and R⁶ are as previously
defined

(xii)aryl, and optionally substituted aryl

(xiii) heteroaryl, and optionally substituted heteroaryl

35 (xiv) C₃-C₇-cycloalkyl

(xv) C₁-C₁₂-alkyl substituted with heteroaryl

(xvi) NHC(O)R^3 where R^3 is as previously defined

(xvii) $\text{NHC(O)NR}^5\text{R}^6$ where R^5 and R^6 are as previously defined

5 (xviii) $=\text{N-NR}^7\text{R}^8$ wherein R^7 and R^8 are as previously defined

(xix) $=\text{N-R}^4$ wherein R^4 is as previously defined,

(xx) $=\text{N-NHC(O)R}^3$ wherein R^3 is as previously defined, and

10 (xxi) $=\text{N-NHC(O)NR}^5\text{R}^6$ wherein R^5 and R^6 are as previously defined,

(5) $\text{C}_2\text{-C}_{10}\text{-alkynyl}$, and

(6) $\text{C}_2\text{-C}_{10}\text{-alkynyl}$ substituted with one or more substituents selected from the group consisting of

(i) halogen,

15 (ii)

OR^4 where R^4 is defined as previously

(iii) -CHO

(iv)

oxo

20 (v) $\text{-CO}_2\text{R}^3$ where R^3 is as previously defined

(vi)

$\text{-C(O)NR}^5\text{R}^6$ wherein R^5 and R^6 are as previously defined

(vii) -CN

25 (viii) NR^7R^8 wherein R^7 and R^8 are as previously defined

(ix) $=\text{N-O-R}^4$ where R^4 is as previously defined

(x) $\text{-S(O)}_n\text{R}^3$ where n and R^3 are as previously defined

(xi) aryl, and optionally substituted aryl

(xii) heteroaryl, and optionally substituted heteroaryl

30 (xiii) $\text{C}_3\text{-C}_7\text{-cycloalkyl}$

(xiv) $\text{C}_1\text{-C}_{12}\text{-alkyl}$ substituted with heteroaryl

(xv) NHC(O)R^3 where R^3 is as previously defined

(xvi) $\text{NHC(O)NR}^5\text{R}^6$ where R^5 and R^6 are as previously defined

35

(xvii) $=\text{N-NR}^7\text{R}^8$ wherein R^7 and R^8 are as previously defined

(xviii) $=N-R^4$ wherein R^4 is as previously defined
(xix) $=N-NHC(O)R^3$ wherein R^3 is as previously defined, and
(xx) $=N-NHC(O)NR^5R^6$ wherein R^5 and R^6 are as previously defined;

5 R^2 is selected from the group consisting of

- (1) hydrogen
- (2) OH
- (3) OR^3 where R^3 is as previously defined
- (4) $OC(O)R^3$ where R^3 is as previously defined, and
- 10 (5) $O(CO)OR^3$ where R^3 is as previously defined;

and X and Y taken together are selected from the group consisting of

- (1) O
- (2) NOR^4 wherein R^4 is as defined previously
- 15 (3) $N-O-C(R^9)(CR^{10})-O-R^4$ where R^4 is as previously defined and

(i) R^9 and R^{10} are each independently defined as R^4 ,
or

(ii) R^9 and R^{10} are taken together with the atom to
20 which they are attached form a C_3 - C_{12} cycloalkyl ring,

- (4) NR^4 wherein R^4 is as previously defined, and
- (5) $N-NR^7R^8$ wherein R^7 and R^8 are as previously defined, or one of X and Y is hydrogen and the other is selected
- 25 from the group consisting of

- (1) $-OR^4$ wherein R^4 is as previously defined, and
- (2) $-NR^7R^8$ wherein R^7 and R^8 are as previously defined.

R^8 is selected from the group consisting of

- (1)
- 30 (2) hydrogen
- (3) R^3 as previously defined

(4) COR^3 where R^3 is as previously defined;

35 subject to the proviso that when the structure is IV, Z and M are part of a five- or six- membered ring, said

rings optionally being fully or partially unsaturated; for the six- membered ring, the bonding between Z and M is through a carbonyl group; for the five- membered ring, the bonding is directly between Z and M excluding CO; Z and M are independently selected from the group consisting of carbon, oxygen or N; and when M = N a second bridge may exist between this nitrogen and the oxygen of the 12-OH group whereby either an additional annulated oxazole or oxazine ring constitutes part of the molecule; and subject to the proviso that when the structure is V', Z and M are part of a five- or six-membered ring, said rings optionally being fully saturated or fully or partially unsaturated; for the six-membered ring, the bonding between Z and M is through a carbonyl group; for the five-membered ring, the bonding is directly between Z and M excluding CO; Z and M are independently selected from the group consisting of carbon, oxygen or nitrogen; and when M = N a second bridge may exist between this nitrogen and the urethane nitrogen.

7. A pharmaceutical composition comprising an antibiotic 10-desmethyl macrolide as claimed in any one of claims 1 to 6 together with at least one pharmaceutical excipient.

8. The use of an antibiotic 10-desmethyl macrolide as claimed in any one of claims 1 to 6 for the manufacture of a medicament for use in the treatment or prevention of infection in animals.

9. A method of treatment of a human or animal subject to combat bacterial infection thereof, which method comprises administering to said subject an antibiotic 10-desmethyl macrolide as claimed in any one of claims 1 to 6.

10. A 6-protected-hydroxy-10-acetyloxymethyl-10,11-unsaturated macrolide analog, for use as an intermediate.